

## REMARKS

Status of the Claims

Claims 1-9 and 15 are pending in this application. Withdrawn claims 10-14 and 16-20 have been cancelled with this Amendment. Claim 1 was amended to expressly recite the point of pegylation and claims 4-9 and 15 have been amended to expressly describe the mixture in which the conjugate is present. Support for amendment to claim 1 can be found, for example, in paragraphs [0042]<sup>1</sup> and [0089]. Support for the amendment to claim 4 can be found, for example, in paragraphs [0050] and [0087]. Support for the amendment to claims 9 and 15, can be found, for example, in paragraph [0079]. Claims 5-8 were amended to directly or indirectly depend from claim 9. Support for the amendment to claims 5 and 6 can be found, for example, in paragraphs [0050]-[0053] and [0061], whereas support for the amendments in claims 7 and 8 can be found, for example, in paragraphs [0055], [0056] and Example 3. Support for new claims 21 and 22 can be found, for example, in the original claim 15 and paragraphs [0052] and [0053], respectively. Support for new claims 23 and 24 can be found, for example, in the original claims 7 and 8, and paragraph [0056]. No new matter has been added.

Rejection Under 35 U.S.C. §112, First Paragraph

Reconsideration is respectfully requested of the rejection of claims 1-9 and 15 under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Office alleged that one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed genus of PEG-linking structure-hGH. Furthermore, it was alleged that the linking structure may be bound at any point to either PEG or hGH, and that a complete conjugated structure is lacking in the claims.

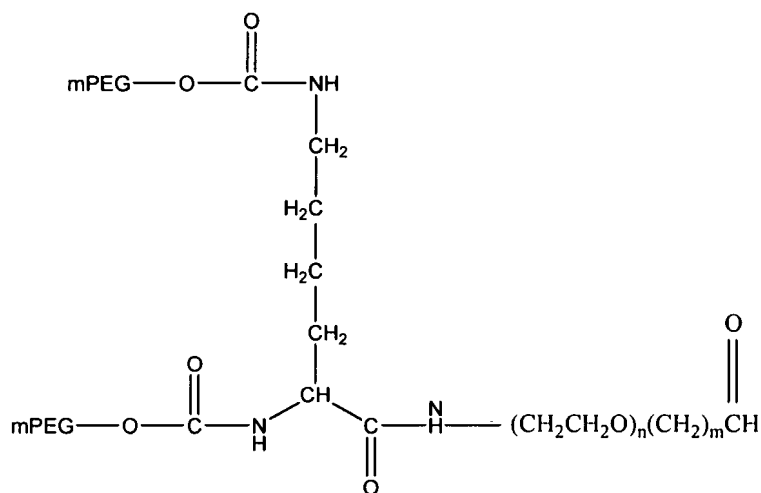
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<sup>1</sup> Paragraph numbering is based on the published U.S. application US 2004/0127417, published on July 1, 2004.

Firstly, it is noted that a complete conjugated structure was provided in the originally filed claims and is also provided in the claims as amended. As amended, claim 1 depicts a conjugated structure of PEG and human growth hormone (hGH) or methionyl hGH, and requires that the hGH or methionyl hGH be monopegylated at its N-terminus. The PEG molecule used in claim 1 is a methoxy-branched PEG aldehyde. Similarly, the amended claim 2 shows a particular species of the PEG-hGH conjugate of claim 1, wherein hGH or methionyl hGH is monopegylated at its N-terminus to methoxy-branched PEG butyraldehyde. In both claims 1 and 2, hGH or methionyl hGH portion of the conjugate is represented by R. Claims 3-9 and 15 depend directly or indirectly from claims 1 or 2, and thus relate to the same structures as discussed above.

Secondly, in view of the amendment to claim 1, Applicants submit that there is no ambiguity as to where the PEG is attached to hGH or methionyl hGH. Specifically, hGH or methionyl hGH is conjugated to a single methoxy-branched PEG aldehyde at its N-terminus. In view of the fact that claims 2-9 and 15 depend from claim 1, they also relate to N-terminally monopegylated hGH shown in claim 1.

Thirdly, the application provides more than ample written description of a number of PEG-hGH conjugates, which would allow one skilled in the art to recognize that the applicant was in possession of the PEG-hGH genus shown in claim 1. Specifically, the PEG-hGH genus of claim 1 includes only hGH or methionyl hGH that is monopegylated at its N-terminus with a methoxy-branched PEG aldehyde of the following structure



wherein  $n$  is an integer between 1 and 10, and  $m$  is an integer between 1 and 10.

Thus, based only on the structure depicted in claim 1, a skilled artisan can readily determine the scope of PEG-hGH conjugates covered therein. In addition, the specification provides detailed information regarding hGH and methionyl hGH that can be used in conjugation reactions (see paragraphs [0040] and [0041]). Also provided is a detailed description of PEG aldehydes that can be used (see, e.g., paragraphs [0055]-[0060]). The conjugation reaction is described, for example, in paragraph [0063]. Furthermore, Example 1 describes a method for generating a substantially homogeneous preparation of N-terminally monopegylated hGH by using a methoxy-branched 40,000MW PEG-butyrylaldehyde. Accordingly, it is respectfully submitted that a skilled artisan would readily recognize that the Applicant was in possession of the claimed PEG-hGH conjugates at the time of filing the application.

Based on the foregoing, Applicants respectfully request withdrawal of the written description rejection.

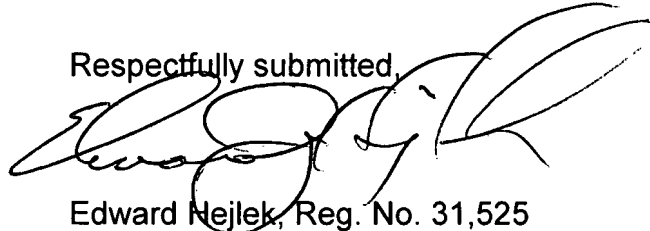
### CONCLUSION

In light of the foregoing, Applicants respectfully request entry of the claim amendments, and solicit an allowance of the claims.

The Examiner is invited to contact the undersigned attorney should any issues remain unresolved.

The Commissioner is hereby authorized to charge \$1,020.00 for a three month extension of time to Deposit Account No. 19-1345.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Edward Hejlek', is written over the typed name and address.

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